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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/099,637	03/15/2002	Gerardo M. Castillo	PROTEO.P16CI	4148

7590 07/13/2004

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EXAMINER	
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ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/099,637	CASTILLO ET AL.	
	Examiner	Art Unit	
	Shaojia A Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2003 and 26 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-15,17 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-15 and 17-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/19/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicant's amendment and response filed on September 11, 2003 and April 26, 2004 wherein claims 1-8 and 16 are cancelled and claims 17-18 are newly submitted.

Currently, claims 9-15 and 17-18 are pending in this application.

Claims 9-15 and 17-18 are examined on the merits herein.

Applicant's declaration of Dr. Alan D. Snow (inventor), submitted September 11, 2003 under 37 CFR 1.132, is acknowledged and will be further discussed below.

Note that claim 10 has been amended in the amendment filed September 11, 2003 and April 26, 2004 by changing to dependent from claim 9, instead of claim 8 in the original claim 10, as Applicant indicates in the Remarks filed September 11, 2003.

Therefore, the objection of claims 10-11 made under 37 CFR 1.75 (c) for improper dependent of record stated in the Office Action dated April 8, 2003 is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention, for the same reasons of record in the Office Action dated April 8, 2003.

The recitation " pharmaceutical acceptable analogs and derivatives" in claims 12-13 render claims 12-13 indefinite. The recitation " pharmaceutical acceptable analogs and derivatives" is not seen to be clearly defined in the specification as to structure, formula, or chemical name. Hence, one of ordinary skill in the art could not ascertain and interpret the metes and bounds as to the recitation "analogs and derivatives" in the claim. Therefore, the scope of claims is indefinite as to the composition encompassed thereby.

Response to Argument

Applicant's arguments filed September 11, 2003 with respect to this rejection made under 35 U.S.C. 112, second paragraph in the previous Office have been fully considered but are not deemed persuasive to overcome this rejection as further discussed below.

Applicant asserts that "pharmaceutical acceptable analogs and derivatives" is well supported in the specification at page 22 where, pharmaceutically acceptable analogs and derivatives" of a claimed compound are disclosed to include various R-group type substitutions and any other derivative structural modification not affecting the disclosed efficacy of these compounds. See page 22 line 31 to page 23 line 2 of the specification. However, Applicant's assertion and the definition of "pharmaceutical acceptable analogs and derivatives" given by the specification at page 22 line 31 to page 23 line 2 are not persuasive as to clearly defining and/or clearly setting forth the

metes and bounds as to "pharmaceutical acceptable analogs and derivatives", since one of ordinary skill in the art could not ascertain what various R- group type substitutions and any other derivative structural modification not affecting the disclosed efficacy of these compounds would be encompassed thereby. Note that the specification fails to define what would be "various R- group type substitutions" and "any other derivative structural modification not affecting the disclosed efficacy of these compounds" as to structure, formula, or chemical name.

Therefore, the claims are indefinite as to the composition encompassed thereby.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9-15 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Kuznicki et al. (5,681,569) for reasons of record stated in the Office Action dated April 8, 2003.

Kuznicki et al. discloses a composition comprising 0.01-0.35% flavanols or catechins wherein the catechin or a mixture of two or more the catechins are catechin, epicatechin, gallocatechin, epigallocatechin gallate and epicatechin gallate (see particularly col.3 lines 20-21 and 26-28), and a pharmaceutical carrier (i.e., water). See also abstract, col.2, lines12-14; Example I, II, and III at col.10, and claims 1 and 5-6.

Kuznicki et al. also discloses the composition therein is therapeutically useful in improving cognitive performance (see col.3 line 33 in particular). The therapeutic effective amount of a catechin or mixture of catechins, within the instant claim (10-100mg/kg of body weight of the subject), is disclosed in the Example I and III (see col. 10 lines 1-41) as shown in the calculation below:

Example III discloses that a person can consume 835 cc (835 ml) of a beverage prepared according to Example I (see col.10 lines 40-41).

Since the water in the composition in Example I is 94.45%, the composition is aqueous solution. The density of water = 1 g/ml, thus the total amount of the composition in Example I is 835 g.

According to Example I, the effective amount of catechins (or flavanols)

= 835g X 0.097% (see col.10 line 15 in particular) = 0.8099 g = 809.9 mg

OR in different calculation, according to Example I (see particularly at col.10 lines 6 and 13-14)

the effective amount of catechins

= 835g X 0.35/100 X 29/100 = 0.8475 g = 847.5 mg.

Since a standard person weight is 70 kg, the range of effective amounts of catechins is 10 mg/kg X 70 kg =<u>700 mg</u> to 1000 mg/kg X 70 kg = <u>70,000 mg</u>.

Thus, the effective amount of catechins as exemplified in Example I in the composition of Kuznicki et al., 809.9 mg or 847.5 mg, is within the instant claimed range.

Kuznicki et al. also discloses that catechins therein are extracted from green teas or other plants, and isolated from green tea by methods well known to those in the art (see particularly at col.4 lines 6-14). Thus, their percentage purity herein is known to significantly exceed a proportion percentage of the catechin presence in a plant, which is an inherent property of the composition of Kuznicki et al. Kuznicki et al. also discloses that catechins can be prepared by synthetic chemical method or commercially available (see col.4 lines 14-17).

Thus, Kuznicki's composition inherently treat amyloid in a mammal. Moreover, the claiming of a new use, new function or unknown property which is inherently present in the prior art does not make the claim patentable. See *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

Thus, Kuznicki et al. anticipates claims 9-15 and 17.

Response to Argument

Applicant's arguments filed September 11, 2003 with respect to this rejection made under 35 U.S.C. 102(b) in the previous Office have been fully considered but they are not deemed persuasive to render the claimed invention patentable over the prior art as further discussed below.

Applicant's arguments that "[T]he disclosures of Kuznicki are not directed to therapeutics for diseases of any sort" and "Kuznicki does NOT address any kind of general cognitive improvement with his formulation, but rather a very specific "increased cognitive performance after heat dehydration", are not persuasive, since the instant

claims are directed to a pharmaceutical composition not a method of treating amyloid disease in a mammal. It has been well settled that recitation of an inherent property of a composition, e.g., "treating amyloid" in claims herein, will not further limit claims drawn to a composition so long as the prior art teaches the composition comprising the same ingredients in the same amount, e.g., the same amount of catechins.

Therefore, Kuznicki's composition is deemed to have the inherent property for treating amyloid in a mammal when administering the Kuznicki's composition to a mammal. Moreover, the claiming of a new use, new function or unknown property which is inherently present in the prior art does not make the claim patentable. See *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

Thus, Kuznicki et al. anticipates claims 9-15 and 17.

Claims 9, 12-15, and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by JP 10245342 for reasons of record stated in the Office Action dated April 8, 2003.

JP 10245342 discloses a pharmaceutical composition for diminishing the toxicity in nerve cells caused by β–amyloid protein comprising a catechin or two or more of catechin such as epigallocatechin gallate and epicatechin gallate prescribed in effective amounts (doses) of diminishing the toxicity of β–amyloid protein (see particularly page 1, the 2nd paragraph; claims 1-3 at page 1; page 2 [0001], [0002]), and a pharmaceutical carrier (i.e., water). See also page 7 [0028]; page 8 [0029]. JP 10245342 also discloses that catechins therein are extracted from teas or other plants, and isolated and purified by HPLC (see page 6 [0027]). Thus, their percentage purity herein is known to

significantly exceed a proportion percentage of the catechin presence in a plant, and substantially pure isolated, which is an inherent property of the composition therein.

Thus, JP 10245342 anticipates claims 9, 12-15, and 17.

Response to Argument

Applicant's arguments and the declaration of Alan Snow under 37 CFR 1.132 filed September 11, 2003 with respect to this rejection made under 35 U.S.C. 102(b) in the previous Office have been fully considered but they are not deemed persuasive to render the claimed invention patentable over the prior art as further discussed below.

Applicant's arguments that "Specifically, there is no way to tell with any certainty that a formulation proposed by Mitsui Norin to reduce amyloid toxicity would also and at the same time necessarily have the effect of inhibiting or reversing amyloid fibrillogenesis, much less alpha-synuclein or NAC tibrillogenesis" are not convincing for the following reasons.

Again, Applicant is reminded that the instant claims are directed to a pharmaceutical composition, not a method of treating amyloid disease in a mammal, nor methods of inhibiting or reversing amyloid fibrillogenesis, much less alpha-synuclein or NAC tibrillogenesis. So long as JP 10245342 discloses the composition comprising the same ingredients in the effective amount of catechins for diminishing the toxicity in nerve cells caused by β–amyloid protein, it meets the claimed limitations. Thus, the prior art composition is deemed to have the inherent property for treating amyloid in a mammal. Moreover, the claiming of a new use, new function or unknown property which

is inherently present in the prior art does not make the claim patentable. See *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

Further, Applicant assertion in the declaration under 37 CFR 1.132 using the reference by Wang that "there are no necessary inferences available as teachings to be applied to Aβ fibrillogenesis from the cited studies pertaining to neuronal cell death, because in at least some of the reported studies, the causes of the cell death do not involve any effect on Aβ sbrillogenesis" and "There is thus no implication available to serve as a teaching that inhibition of nerve cell death or nerve cell toxicity by Aβ inherently leads to inhibition of Aβ fibril formation, deposition, accumulation and/or persistence" have been fully considered but not found convincing.

First, as indicated above, the instant claims are not a method claims. Second, even if the method of treatment were claimed herein, the mechanism of action of a treatment does not have a bearing on the patentability of the invention if the claimed method steps are already known even though applicant has proposed or claimed the mechanism. Third, the declaration merely presents statements or inferences or inconclusive mechanistic studies, but fails to set forth any factual evidences. Therefore, the declaration of Snow is not persuasive to rebut the prima facie case herein.

Thus, JP 10245342 anticipates claims 9, 12-15, and 17.

The following is new rejection(s) necessitated by Applicant's amendment filed on September 11, 2003 and April 26, 2004, wherein new claim 18 has been added.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kuznicki et al. (5,681,569) or JP 10245342.

The same disclosure of Kuznicki et al. (5,681,569) or JP 10245342 has been discussed in the 102(b) rejections in the previous Office Action or above.

The cited prior art does not expressly disclose a drug product comprising a container labeled or accompanied by a label indicating that drug product for treating amyloid in a mammal and the container containing the same catechin composition.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to prepare a container labeled or accompanied by a label indicating that drug product for treating amyloid in a mammal and the container containing the same catechin composition.

One having ordinary skill in the art at the time the invention was made would have been motivated to prepare a container labeled or accompanied by a label indicating that drug product for treating amyloid in a mammal and the container containing the same catechin composition, since that the inclusion of a package or container inserts including "indication and use" of the pharmaceutical composition is

mandated by 21 CFR 201.57 according to *Remington: The Science and Practice of Pharmacy*. Moreover, the inclusion of a package or a container inserts including "indication and use" of the pharmaceutical composition is considered well within conventional skills in pharmaceutical science.

Moreover, with respect to the instructions that direct one on how to use in a kit or a drug product as Applicant asserts, the U.S. Court of Appeals for the Federal Circuit, *In re Ngai* 03-1524, recently rules that a kit of the prior art with a set of instructions is unpatentable (see the precedential opinion issued May 13, 2004).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 9 and 12 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 14-15 of the copending Application No. 09/748,748 for reasons of record stated in the Office Action dated April 8, 2003. .

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending Application is drawn to a drug product containing a composition for treating α–synclein fibril formation comprising a compound of Formula E which is epicatechin (see Fig. 1B herein) and a pharmaceutically acceptable excipient. The claim of the instant application is drawn to a pharmaceutical composition for treating α–synclein fibril formation comprising epicatechin and a pharmaceutically acceptable excipients of the patent in amounts within the copending Application claim.

Therefore, one of ordinary skill in the art would have found that the instant composition is clearly obvious in view of the copending Application No. 09/748,748.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Note that Applicant states that "Applicant submits in response that it will file the appropriate terminal disclaimer upon an indication of allowable subject matter in this case" in the Applicant's Remarks filed September 11, 2003 (see page 8 the first paragraph).

In view of the rejections to the pending claims set forth above, no claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703.872.9307.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
July 2, 2004

SHAOJIA ANNA JIANG
PATENT EXAMINER